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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,747	10/16/2003	Helen M. Blau	SUPP-P01-011	1982

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EXAMINER

LI, QIAN JANICE

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/688,747	Applicant(s) BLAU ET AL.	
	Examiner Q. Janice Li, M.D.	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 1-33 and 35-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34, 39 and 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 October 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, claims 34, 39, and 40, is acknowledged. The traversal is on the ground(s) that all three groups contain the limitation of treating neuronal deficiency, and that a search of these claims can be made without serious burden. This is not found persuasive because it is maintained that each of the Inventions requires a separate search status and technical consideration. The inventions are mutually exclusive and independent methods for treating neuronal deficiencies. For example, the method of group I comprises bone marrow transplantation, which is not required in the method of group III. Likewise, the bone marrow mobilization therapy is not required in the method of group I. Thus, the different methods use completely different starting materials and protocols. As such, the Invention of group III requires different reagents, steps, protocols, search criteria, and technical considerations than the Invention of group I. The searches for all three groups would have certain overlap, but they are not co-extensive. M.P.E.P. states, "FOR PURPOSES OF THE INITIAL REQUIREMENT, A SERIOUS BURDEN ON THE EXAMINER MAY BE PRIMA FACIE SHOWN IF THE EXAMINER SHOWS BY APPROPRIATE EXPLANATION OF SEPARATE CLASSIFICATION, OR SEPARATE STATUS IN THE ART, OR A DIFFERENT FIELD OF SEARCH AS DEFINED IN MPEP § 808.02". Therefore, it is maintained that these inventions are distinct due to their divergent subject matter. Further search of these inventions is not co-extensive, as indicated by

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the separate classifications. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-40 are pending, however, claims 1-33, 35-38 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 34, 39, and 40 are under current examination.

Drawings

The patent or application file contains at least one drawing executed in color. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34, 39, 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the nature of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

The claims are drawn to treating a neuronal deficiency comprising administering a bone marrow cell mobilization therapy. The specification reviews the types of neuronal deficiency that could be treated by the instantly claimed invention, which include almost every known neurological disease, ranging from congenital neural deficiency to Parkinson's. The specification teaches that the inventors have found that bone marrow-derived cells are capable of entering the nervous system and forming bone marrow derived neurons, and then contemplates using such approach for regeneration of neurons and treating neuronal disorders. The specification prophetically states that these diseases could be treated with a bone marrow cell mobilization treatment (paragraph 0089), and refers to prior art for details of the treatment citing *Chao et al*, (Blood, 1993), who administered G-CSF to "mobilize" macrophages and platelets for promoting bone marrow recovery from high dose chemotherapy. However, *Chao et al* use G-CSF in a completely different circumstance where the patient underwent chemotherapy and administering growth factor G-CSF promoted regeneration of new blood cells. *Chao* reference does not provide any teaching regarding treating a neuronal disease/symptom, and thus cannot substitute a specific guidance for practicing instantly claimed invention for treating neuronal deficiency. The specification fails to provide any details or reduce to practice concerning how to use a bone marrow mobilization therapy for ameliorating any one symptom of any one neuronal deficiency, and thus fails to provide an enabling disclosure for what is now claimed.

Turning to the state of the art, although it had become known at around time of instant filing that bone marrow cells have the potential to differentiate into neuronal cells

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(*Kopen et al*, PNAS 1999;96:10711-6; *Sanchez-Ramos et al*, Exp Neurol 2000;164:247-56; *Mezey et al*, Science 2000;290:1779-82), which has the potential for neuron regeneration, the state of the art was in the infant stage of development, and the bone marrow mobilization treatment or bone marrow transplantation was far from treating any neuronal diseases. For example, five years after instant filing date, *Sigurjonsson et al* (PNAS 205;102:5227-32) teach "ADULT HSCs FROM RODENTS AND HUMANS INJECTED INTRAVENOUSLY OR INTRACEREBRALLY INTO RODENT HOSTS CAN SETTLE IN THE BRAIN AND EXPRESS NEURONAL MARKERS, BUT THE INCIDENCE OF NEURONAL DIFFERENTIATION HAS NEVER BEEN REPORTED TO EXCEED 1-2% OF THOSE HSCs THAT INTEGRATE INTO THE BRAIN" and "THE CHARACTERIZATION OF NEURONAL PHENOTYPE IN ALL THESE STUDIES HAS BEEN LIMITED TO THE EXPRESSION OF SELECTED MOLECULAR MARKERS. FUNCTIONAL PHENOTYPIC FEATURES AND INTEGRATION INTO SYNAPTIC NETWORKS HAVE NOT BEEN DEMONSTRATED" (column 2, page 5227, emphasis added). Clearly, at such a low rate of neuronal differentiation, and uncertainty of neuron phenotype and function, any therapeutic effect of mobilized BMDCs on treating a neuronal deficiency would be remote. In a post-filing publication, instant inventor concurs (*Pomerantz & Blau*, Nat Cell Biol 2004;6:810-6), "MAJOR CHALLENGES EXIST IN THE USE OF BMDCs IN A CELL-BASED THERAPY FOR NON-HEMATOPOIETIC TISSUES, INCLUDING INCREASING THEIR EFFICIENCY OF INCORPORATION INTO TARGET TISSUES AND DEMONSTRATING EFFICACY IN TREATING TISSUE MALFUNCTION" (column 2, page 810). The authors are optimistic for the emerging potential of BMDCs, but the reality was, and still is, that the state of the pertinent art has not developed to the extent that enabling a therapeutic use for ameliorating any symptom of a neuronal disorder at the time of instant priority date.

In light of the state of the art as discussed *supra*, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for the claimed invention. Although the instant specification provides preliminary studies on migration, relocation, and contribution of transplanted BMDCs to Purkinje neurons in the brain, it fails to teach whether a BM cell mobilization therapy would boost relocation of bone marrow cells to the brain, and cause their differentiation into neurons. The specification fails to teach the efficacy of such BM mobilization processes, whether it is sufficient to the extent that any clinical benefit could be observed.

Moreover, the observation of neuronal differentiation occurred in the circumstance where the recipient received lethal irradiation before BM cell transplantation, where instant claims are drawn to administering cytokines G-CSF/GM-CSF without any cell transplantation. It is unknown, unpredictable, and the specification fails to teach whether the neuronal differentiation would occur just giving a growth factor G-CSF. Accordingly, the specification fails to provide an enabling disclosure for what is now claimed.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34, 39, 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are vague and indefinite because they fail to clearly set forth the method step(s). The method provides for administering "a bone marrow mobilization therapy", however, there is no step clearly set forth the therapeutic regimen. It is unclear what step the "mobilization therapy" includes, and thus the metes and bounds of the claims are unclear. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

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Any inquiry of formal matters can be directed to the patent analyst, **William Phillips**, whose telephone number is (571) 272-0548.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

**Q. JANICE LI, M.D.
PRIMARY EXAMINER**



Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL

May 1, 2006